IN THE CLAIMS

Please amend claims 1, 3-6, 12, 13, 16 and 36 as follows (*A marked-up copy of the amended claims is provided in an Appendix attached to this Response*):

1. (Amended) A knockin non-human gene-mutated animal having a mutant presenilin-1 gene.

3. (Amended) A knockin non-human gene-mutated animal having a mutant presenilin-1 gene which comprises a DNA having a sequence encoding a mutant presenilin-1 protein which has an amino acid sequence in which one or more amino acids at positions selected from the group consisting of amino acids numbers 79, 82, 96, 115, 120, 135, 139, 143, 146, 163, 209, 213, 231, 235, 246, 250, 260, 263, 264, 267, 269, 280, 285, 286, 290, 318, 384, 392, 410, 426 and 436 is substituted with different amino acids in the amino acid sequences of presenilin-1 protein.

4. (Amended) A knockin non-human gene-mutated animal having a mutant presenilin-1 gene which comprises a DNA having a sequence encoding a mutant presenilin-1 protein which has one or more mutations selected from the group consisting of A79V, V82L, V96F, Y115H, Y115C, E120K, E120D, N135D, M139V, M139T, M139I, I143F, I143T, M146L, M146V, H163Y, H163R G209V, I213T, A231T, A231V, L235P, A246E, L250S, A260V, C263R, P264L, P267S, R269G, R269H, E280A, A285V, L286V, S290C, E318G, G384A, L392V, C410Y, A426P and P436S in the amino acid sequences of presenilin-1 protein, wherein each alphabet represents an amino acid expressed as a one-letter symbol, each number represents an amino acid number from the n-terminus of the presenilin-1 protein, and the descriptions means that a wild-type amino acid shown in the left of the number is substituted with an amino acid shown on the right.

5. (Amended) A knockin non-human gene-mutated animal having a mutant presenilin-1 gene which comprises a DNA having a sequence encoding a mutant presenilin-1 protein in which isoleucine at position 213 of a presenilin-1 protein is substituted with an amino acid other than isoleucine.

6. (Amended) A knockin non-human gene-mutated animal having a mutant presenilin-1 gene which comprises a DNA having a sequence encoding a mutant presenilin-1 protein in which isoleucine at position 213 of a presenilin-1 protein is substituted with threonine.

12. (Twice Amended) The gene-mutated animal according to claim 1, wherein the mutant presenilin-1 results in overexpression of amyloid β protein.

13. (Twice Amended) The non-human gene-mutated animal according to claim 1, wherein the animal can express a mutant presenilin-1 protein and wherein the expression of said protein induces the production of amyloid β protein in an amount sufficient to form a progressive neural disease in a peripheral portion of the cerebral cortex of the brain of the animal.

16. (Twice Amended) The non-human gene-mutated animal according to claim 1, wherein the presenilin-1 gene is transferred by homologous recombination.

36. (Twice Amended) A method for evaluating the therapeutic effect or preventive treatment of a substance on Alzheimer's disease, which comprises:

administering a test substance to a gene-mutated animal according to claim 1, then determining a total amount of amyloid β in the brain (M) and the amount of amyloid β 40 and amyloid β 42 in the brain, then calculating a ratio of amyloid β 42/amyloid β 40 (P);